

Application For Research Grant

Date: **January 3, 1958**

1. Name of Investigator: **Roe B. Wells, Jr., M.D.**
2. Title: **Associate in Medicine, Peter Bent Brigham Hospital;
Clinic Associate in Medicine, Harvard Medical School;
Director of Chest Clinic and Pulmonary Function Laboratory,
Peter Bent Brigham Hospital.**
3. Institution
& Address: **Peter Bent Brigham Hospital
721 Huntington Avenue
Boston 15, Massachusetts**
4. Project or Subject: **A Study of the Correlation of Smoking History and Habits with
Pulmonary Function and the Acute Effects of Smoking Thereon in Patients with
Bronchitis, Bronchial Asthma, and the Common Cold with Similar Studies in a
Selected Geriatric Population of Apparent Good Health.**
5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

Rationale

This laboratory has recently completed studies of the effects of smoking upon pulmonary function. The majority of these patients were individuals with advanced chronic pulmonary disease. It is felt that a similar analysis is needed in the more common or reversible respiratory ailments such as bronchitis, bronchial (not cardiac) asthma and the common cold, since it is in these individuals that the physician lacks sufficient evidence regarding the role played by cigarette smoking. Such patients represent the major work load of this laboratory and its associated Chest Clinic.

As part of renewed interest in the process of aging, there is a well established geriatric clinic where an intensive study of the older members of the population is being carried on. This study includes studies of the respiratory system.

The facilities of the pulmonary function laboratory and the geriatric clinic afford rich opportunity to correlate smoking history and habits, and acute respiratory disease with pulmonary function.

Method of Study

All patients to be studied will have a complete medical history, physical examination, and routine laboratory procedures including blood count, urinalysis, chest-x-ray, and electrocardiogram. (Continued on page 1 a.)

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A detailed history of smoking habits will be recorded on a protocol sheet prior to testing. This will include the total duration of smoking or chewing of tobacco of any kind, periods of interruption, relationship to time of day, prior illnesses, activities or stress and individual method of smoking, i.e., what portion is discarded, what holders or filters may be used and under what environmental conditions is the smoke inspired. (We have found it of value to corroborate or amplify these details with at least one member of the patient's family in a separate interview.) Finally the patient's attitude toward his smoking is explored. He is asked why he smokes, why he started, has he tried to stop, and has his opinion about smoking ever changed.

Patients studied will be in a comfortable seated position, usually in the fasting state, specifically not earlier than two hours after the last meal. The standard lung volumes are recorded on a closed circuit high speed spirometer and when appropriate, include determination of residual volume by the closed circuit helium method. Following this, the intra-esophageal balloon technique is used to measure mean pulmonary airway resistance and pulmonary compliance. This is also done with a closed circuit system, recording tidal volume by way of a rotational potentiometer attached to the spirometer and led into a recording galvanometer. On the same time axis is the recording from a transducer of the intra-esophageal pressure (adapted from the original method of Mead and Whittenberger). If the clinical history, examination, or routine laboratory data suggest any cause for arterial oxyhemoglobin unsaturation, arterial blood samples will be obtained from an indwelling arterial needle (brachial or radial).

Following these baseline studies (roughly 10 - 15 minutes excluding the residual volume) the patient smokes one cigarette in the manner in which he is accustomed. The method, amount, and duration of smoking are noted and recorded. The above procedure of mean airway resistance determination is repeated at once and again in 7 to 8 minutes after cessation of smoking. With an oscilloscope wired from the recording galvanometers changes in airway resistance are noted at once. On the basis of these observations the cigarette smoking is repeated once again (within 10 minutes) or a nebulized bronchodilator (Isoproterenol) administered. If this latter agent is effective, its preventive abilities are evaluated by repeating the cigarette smoking at various intervals up to 45 minutes. (The various times reported here (7 to 8 minutes, 45 minutes, etc.) are derived from prior experience in this laboratory as the most comprehensive periods for recording the various effects).

Studies in the geriatric study group will follow the same pattern. The other studies of these patients mentioned above will be integrated when appropriate with the data on smoking.

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1st year.	End yr.		3rd yr.	Total 3 yrs.
6. Budget Plan:				
\$2,000.00	\$2,000.00	Salaries	\$2,000.00	\$6,000
750.00	750.00	Expendable Supplies	750.00	2,250
4,760.00	850.00	Permanent Equipment		5,610
1,877.50	900.00	Overhead 25%	687.50	3,465
		Other		
\$9,387.50	\$4,500.00		\$3,437.50 Total	17,325

* As prescribed by the Trustees of the Institution.

7. Anticipated Duration of Work: Three years (July 1, 1958 to June 30, 1961)

8. Facilities and Staff Available: Pulmonary Function Laboratory of a 286 medical-surgical bed hospital. The laboratory is equipped to carry out determinations of all lung volumes, mechanical factors of respiration, blood and respiratory gas analyses and their tensions, pH, intra-vascular and thoracic pressures, as well as the various compartments and functions derived from these, such as respiratory dead space, alveolar arterial oxygen gradients and respiratory responses to inhalation of various gas mixtures. Fluoroscopy and x-ray facilities are immediately adjacent. (Continued on page 2 a.)

9. Additional Requirements: None

10. Additional Information (Including relation of work to other projects and other sources of supply):

The relation of this proposed study to other work is answered in part under the protocol of item 5 above. Besides the geriatric study, the other study now in progress in this laboratory and also referred to above involves the study of sputum viscosity, primarily in relation to high humidity therapy (steam or fog) and the effect of various agents upon sputum production and character.

In regard to other projects outside the hospital we have followed with interest the reports from Dr. J. Howland Auchincloss of Syracuse and through personal communication the work of Dr. Ernest Attinger in this related field. Concerning the basic methodology there is constant liaison with the Department of Physiology of the Harvard School of Public Health wherein excellent work in the general field of the mechanics of respiration is being carried out. (This group has studied 5 smokers over the age of 50 and found an elevated airway resistance in 4.) (Continued on page 2 a.)

Signature /s/ R. B. Wells
Director of Project

/s/ Victoria Caas M. D.

Business Officer of the Institution

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5 physicians

3 full-time (1 laboratory director 2 research fellows)
2 part-time (1 cardiologist 1 chest physician)

Active cooperation and collaboration with members of the Thoracic Service.

1 senior technician (10 years experience as cardiopulmonary technician)

1 technician-secretary

10. continued

For 1958-1961 there are no other sources of supply regarding the laboratory other than the very small remainder (less than \$300) of the funds that were provided to establish the laboratory some time ago. The laboratory director is supported by the Howard Hughes Medical Institute.

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